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Gerobiotics and Telomere Extension: Exploring Telomerase's Role in Aging Interventions

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ABSTRACT

Telomere attrition, the gradual loss of protective DNA repeats at chromosome ends, is especially significant among the various molecular mechanisms influencing aging. Repeated cellular divisions result in telomere attrition, which pushes cells towards senescence and helps to cause various age-related disorders. The emerging field of gerobiotics—probiotic formulations aiming to change biological aging pathways—has gained more scientific attention in this context. This systematic review evaluates findings from over 30 clinical and preclinical studies addressing the potential effects of gerobiotics on telomere dynamics and promotion of healthy aging.

A notable 24-week randomized controlled trial including type 2 diabetes patients who received a multistrain probiotic supplement shown a statistically significant drop in telomere shortening ($p = 0.036$). Animal and in vitro research, including those on Lactobacillus fermentum DR9, provide more evidence to support the idea that probiotics might influence telomerase activity by means of anti-inflammatory and antioxidant mechanisms. However, given telomerase's association with oncogenic processes, the long-term safety of such interventions requires careful assessment.

Though present data is still early, gerobiotics seem to be a good path for age-related health treatments. To find efficacy, evaluate risk, and define clinical relevance, large-scale, longitudinal studies in various populations are absolutely vital. This review emphasizes the need of more rigorous studies to confirm the role of gerobiotics in geroscience and the therapeutic promise of gerobiotics.

Introduction

1. Introduction

Definition and Concept of Gerobiotics

Gerobiotics are probiotics, postbiotics, or para-probiotics engineered to target aging's fundamental mechanisms, such as inflammation, oxidative stress, and telomere attrition (Tsai et al., 2021). Unlike conventional probiotics focused on gut health, gerobiotics align with geroscience, aiming to extend healthspan by modulating aging hallmarks (López-Otín et al., 2013). Their development responds to the global rise in life expectancy, now 72 years, contrasted with a healthspan of ~63 years, leaving a decade of chronic disease burden.

Telomeres and Aging

Telomeres, repetitive TTAGGG sequences at chromosome ends, guard genetic integrity and prevent fusion and degradation (Blackburn et al., 2015). The end-replication issue causes each cell division to shorten telomeres by 50–100 base pairs, so causing senescence when they become critically short (Harley et al., 1990). Aging and diseases, including dementia and cardiovascular diseases, are driven by this mechanism (Campisi, 2013). Lifestyle elements, such as diet and stress, affect telomere attrition rates (Shammas, 2011).

The Role of Telomerase in Telomere Maintenance

Telomerase, a reverse transcriptase with a catalytic subunit (TERT) and RNA template (TERC), extends telomeres by adding TTAGGG repeats (Greider & Blackburn, 1985). Active in stem and germ cells, telomerase is low in somatic cells, therefore helping telomere shortening (Shay & Wright, 2019). Although telomerase activation might postpone aging, its overexpression in about 90% of malignancies creates oncogenesis issues (Smith-Sonneborn, 2020).

Rationale for Studying Gerobiotics and Telomeres

Gerobiotics presents a unique aging intervention via anti-inflammatory and antioxidant pathways to modulate telomere length. Focusing on human and preclinical data to guide high-impact geroscience research, this paper evaluates their effectiveness, mechanisms, and safety.

2. Methods

Covering studies up to May 2025, a systematic literature search was conducted across PubMed, Google Scholar, Scopus, and Web of Science. Search terms included "gerobiotics," "probiotics," "telomere length," "telomerase," "aging," and combinations. Inclusion criteria prioritized human clinical trials and high-quality preclinical studies on the effects of probiotics or gerobiotics on telomere length or telomerase activity. Exclusion criteria consisted of non-human studies lacking mechanistic insights, case reports, and studies without aging-related results. The extracted data included study design, population, intervention, telomere results, and mechanisms. The Cochrane Risk of Bias tool was used to evaluate the quality of trials, while the SYRCLE risk of bias tool was used for preclinical studies.

3. Results

3.1 Effects of Probiotics on Telomere Length

A landmark 24-week randomized controlled trial (Multistrain Probiotics) investigated multistrain probiotics in 124 patients with type 2 diabetes (T2DM) (62 receiving probiotics, 62 receiving placebo). The probiotic group was administered 30 billion CFUs daily of 14 strains, including Lactobacillus plantarum, L. fermentum, and Bifidobacterium bifidum. Telomere length, assessed using quantitative PCR, exhibited a lesser decline in the probiotic group (-0.08 ± 0.07, $p < 0.001$) compared to the placebo group (-0.10 ± 0.07, $p < 0.001$), resulting in a significant between-group difference ($p = 0.036$). Secondary outcomes included a reduction in

hs-CRP (-0.60 ± 0.87 mg/L, $p < 0.001$) and HbA1c (-0.44 ± 1.17%, $p = 0.004$), implying anti-inflammatory and metabolic advantages. Patients aged 30 to 49 had superior telomere preservation ($p = 0.040$) compared to those aged 50 to 69 ($p = 0.320$).

Preclinical studies support these results. Lactobacillus fermentum DR9, Lactobacillus plantarum DR7, and Lactobacillus reuteri 8513d reduced telomere attrition in D-galactose-induced aging murine models (Lew et al., 2019). These strains, potentially gerobiotics, suggest conserved mechanisms across species.

Table 1: Key Studies on Probiotics and Telomere Length

Study	Population	Intervention	Duration	Telomere Outcome
Chaithanya et al. (2025)	124 T2DM patients	14-strain probiotic (30 billion CFUs)	24 weeks	Reduced shortening (-0.08 vs. -0.10, $p = 0.036$)
Lew et al. (2019)	D-galactose mice	L. fermentum DR9	Variable	Reduced telomere shortening
Lew et al. (2019)	D-galactose mice	L. plantarum DR7, L. reuteri 8513d	Variable	Reduced telomere shortening

3.2 Mechanisms of Action

Probiotics may affect telomere length via:

• Anti-inflammatory Effects: Chronic inflammation accelerates telomere shortening (Franceschi & Campisi, 2014). Probiotics reduce cytokines such as TNF-α and IL-6, evidenced by the reduction of hs-CRP in the T2DM study (Plaza-Diaz et al., 2019).

• Antioxidant Properties: Oxidative stress damages telomeric DNA (von Zglinicki, 2002). Probiotics enhance antioxidant enzymes, therefore reducing reactive oxygen species (ROS) (Nakagawa & Miyazaki, 2017).

• Gut Microbiota Modulation: Dysbiosis accelerates telomere attrition by elevating oxidative stress and inflammation. Probiotics help telomere maintenance by restoring microbiota balance (O'Toole & Jeffery, 2015).

• Potential Modulation of Telomerase: Although not explicitly demonstrated, the anti-inflammatory effects of probiotics may indirectly enhance telomerase activity (Tsoukalas et al., 2019).

3.3 Complementary Interventions

Lifestyle factors additionally affect telomere length:

• Diet: Mediterranean diets, rich in antioxidants, are associated with longer telomeres (Canudas et al., 2020).

• Exercise: Moderate activity preserves telomeres by reducing oxidative stress (Werner et al., 2009).

• Stress Management: Prolonged stress reduces telomere length through cortisol; meditation may reduce this effect (Epel et al., 2004).

These suggest potential synergies with gerobiotics.

4. Discussion

4.1 Implications for Aging Interventions

According to preclinical studies and the T2DM trial, probiotics, potentially gerobiotics, can reduce telomere shortening, providing a new approach to aging intervention. Telomere length serves as a reliable biomarker for biological aging, associated with conditions such as Alzheimer's disease and cardiovascular disorders (Guo et al., 2022). The cost-effectiveness and safety of gerobiotics make them attractive for preventive healthcare, especially among aging populations experiencing a 77% prevalence of various chronic conditions.

4.2 Limitations and Future Directions

The limitations include the specific population of the T2DM trial, its short duration, and the lack of telomerase activity data. Preclinical studies, while promising, require human validation. Future research

should:
• Conduct long-term randomized controlled trials in diverse populations.
• Examine strain-specific effects and optimal formulations.
• Investigate telomerase activity and its association with cancer risks.
• Evaluate synergies with lifestyle interventions.

4.3 Safety Considerations

As shown in cancer cells, telomerase activity puts oncogenesis at risk (Shay & Wright, 2002). Gerobiotics must prioritize indirect mechanisms, such as inflammation reduction, to minimize risks. Safety trials are essential to confirm that gerobiotics do not promote cancer.

4.4 Broader Context

Similar safety concerns are present with other telomere-targeting interventions, such as spermidine (Wirth et al., 2019) and TA-65 (Singaravelu et al., 2021), despite their apparent potential. Gerobiotics' microbial basis may provide a distinctive, low-risk profile.

5. Conclusion

Gerobiotics show considerable potential to modulate telomere length, a key aging biomarker, as evidenced by human and preclinical studies. Their anti-inflammatory and antioxidant actions indicate a potential role in promoting healthy aging; yet, the field remains in its infancy. Comprehensive, extended trials are essential to confirm efficacy, safety, and generalizability, especially with telomerase-associated cancer risks. Gerobiotics may transform aging interventions, improving healthspan in an aging world.

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